UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/164,568	10/01/1998	RANDOLPH J. NOELLE	012712-572	6823

909 7590 07/28/2003

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/28/2003

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/164,568	Applicant(s) VOELZ
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5/30/03

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application. 54-56, 58-63

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected. 54-56, 58-63

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☒ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

PAPER NO. 21

DETAILED ACTION

1. Applicant's reply, filed 5/30/03 (Paper No. 20), has been entered.

Claims 54-56 and 58-63, as they read on "autoantigen expressing cells" are being acted upon as the elected invention.

Claims 1-53 and 57 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 5/30/03 (Paper No. 20). The rejections of record can be found in the previous Office Action (Paper No.).

3. Claims 54-56 and 58-63 stand rejected under 35 U.S.C. § 103 as being unpatentable over Lederman et al. (U.S. Patent No. 6,403,091) OR Armitage et al. (U.S. Patent No. 6,264,951) OR Aruffo et al. (U.S. Patent No. 6,376,459) in view of Berschorner et al. (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 5,690,933) and Enyon et al. (J. Exp. Med. 175: 131-138, 1992) for the reasons of record.

Applicant's arguments, filed 5/30/03 (Paper No. 20), have been fully considered but are not found convincing essentially for the reasons of record..

Applicant's comments on the previous issues raised about enablement are acknowledged, however applicant is reminded that the current rejection has been deemed warranted during the prosecution of this patent application.

Applicant argues that the prior art did not provide sufficient motivation and expectation of success at the time the invention was made for the claimed methods.

While applicant acknowledges that Enyon suggest a role for B cell as antigen-specific tolerizing antigen-presenting cells, applicant asserts that Enyon's experimental results are limited to a demonstration of tolerance to a foreign antigen in animals pre-treated with to the same antigen. Applicant asserts that Enyon suggest but does not show that B cells may also maintain peripheral tolerance in a similar manner. Also, applicant asserts that Enyon's studies reveal an in vivo role for B cell-mediated tolerance, which is not predictably extrapolated to a successful method of treatment via administration of autoantigen expressing cells.

Applicant asserts that Beschorner's teachings are limited to therapeutic administration of antigen and APCs only in the context of thymic depletion.

Applicant asserts that Cobbold is limited to induction of tolerance to a self-antigen by administering a CD4-specific antibody, optionally in combination with an immunosuppressive agent and do not teach or suggest the use of gp39-specific antagonists.

Applicant asserts that the proposed combination of teachings is implausible as having no reasonable chance of success. For example and in particular, the term "immunosuppressant" is a generic term that encompasses agents having substantially different in vivo effects (e.g thymic depletion of APCs or interference of CD4 signaling). Applicant asserts that combination of substantially different individual therapies to thereby result in another successful therapy cannot be predicted and that the mere existence of a variety of therapies generally directed to immunosuppression does not motivate any particular combination based on an anticipation of success.

Contrary to applicant's assertions that teachings of Enyon, Beschorner and Cobbold do not support a general conclusion that APCs can be administered to induce tolerance with gp39-specific antagonists with sufficient motivation and expectation of success at the time the invention was made, the following of record is noted.

Enyon et al. teach that B cell presentation of antigen in the absence of appropriate help leads to antigen-specific T cell anergy in vivo (see entire document). Here, Enyon et al. also acknowledge the art-known role of B cells as APCs. It was also known that CD40 the ligand for gp39 (CD40 ligand) is present on other APCs such as dendritic cells, which are intimately involved in the induction of T cell immunity or tolerance. In addition, gp39 was known to be expressed mainly by activated T helper cells and a number of $CD8^+$ cells as well. Therefore, it was known that one could use gp39 antagonists to block T cell-mediated activation and that the appropriate in vivo APCs such as B cells and dendritic cells, which express CD40, would be subject to such manipulation. It was well known in the art at time the invention was made that the provision of signal 1 (antigen) in the absence of signal 2 (help) would lead to some form of tolerance rather than immunity. Enyon et al. also teach a role for small B cells as antigen-specific tolerizing antigen-presenting cells in acquired self-tolerance soluble self-proteins (see Abstract and last paragraph of Discussion).

Berschorner teach the use of antigen containing antigen-presenting cells for inducing tolerance to autoantigens or self antigens in the treatment of autoimmune diseases by administering the said antigen containing antigen presenting cells and an immunosuppressive (see entire document, including Detailed Description and Claims). Beschorner also teach that the antigen presenting cells include dendritic cells, Langerhans cells and mononuclear phagocytes (see column 6, paragraph 3), encompassed by the claimed methods.

Cobbold et al. teach that specific non-responsiveness can be induced to a self antigen or antigens in order to treat autoimmune diseases by administering immunosuppressive antibodies and antigen (see entire document, including column 3, paragraph 4). Cobbold et al. also note that persistent antigen is require to maintain tolerance, which applies to self (auto) antigens in the treatment of autoimmune diseases (column 3, paragraph 5).

As indicated above, applicant acknowledges that APCs can provide antigen to induce tolerance or specific non-responsiveness in various contexts and systems at the time the invention was made.

Contrary to applicant's assertions, the prior art provide sufficient motivation and expectation of success that providing an immunosuppressive regimen, including antagonistic antibodies, in combination with APCs can induce tolerance or antigen-specific nonresponsiveness.

Here, the teachings of Lederman et al., Armitage et al. and Aruffo et al. are clearly drawn to providing antagonists of the immune response to treat various disease conditions, such as autoimmunity. These teachings are consistent with the teachings of Enyon, Beschorner and Waldmann to provide APC's to induce tolerance to antigens of interest under the cover of immunosuppression at the time the invention was made.

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the teachings of the primary references pertaining to the treatment of disease conditions such as autoimmunity and the teachings of the secondary references indicating the success of employing APCs to induce tolerance or specific antigen to solve a similar problem of treating autoimmunity would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art of inducing long term non-responsiveness to autoantigens in such individuals having autoimmunity. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to select the combination of an autoantigen containing antigen presenting cells and a gp39-specific antagonist to induce antigen-specific non-responsiveness to autoantigens as a treatment for autoimmunity by providing persistent autoantigens under the cover of immunosuppressives, since both contribute to long term antigen non-responsiveness in the treatment of autoimmunity.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
July 24, 2003